

P193 **AHRR GENOTYPES PREDICT SUSCEPTIBILITY TO DIOXIN-LIKE CHEMICALS IN CYTOCHROME P450 1A2 INDUCTION IN HUMANS**

Wan-Ting Hung,¹ Ping-Wei Huang,² George H Lambert,³ Larry L Needham,⁴ Donald G Patterson,⁵ Yue Leon Guo¹ *¹College of Medicine NTU, Taipei, Taiwan; ²College of Public Health NTU, Taipei, Taiwan; ³Robert Wood Johnson Medical School, New Jersey, USA; ⁴Centers for Disease Control and Prevention, Georgia, USA; ⁵EnvironSolutions Consulting Inc, Georgia, USA*

10.1136/oemed-2011-100382.407

Objectives Dioxin-like chemicals are known to exert their effect by binding to aryl hydrocarbon receptor (AhR), forming complexes with aryl hydrocarbon nuclear translocator (ARNT), and binding to specific dioxin responsive elements in promoter region to regulate the transcription of specific genes. In human, induction of cytochrome P450 (CYP) family of enzymes is well documented. In previous study, CYP1A2 induction had been reported to be an excellent biomarker of dioxin exposure and human health effects in people highly exposed to dioxin-like chemicals, the Yucheng cohort. The goal of this study is to examine the relationship between inducibility of CYP1A2 and genetic polymorphisms of AhR, ARNT, and AhRR in human.

Methods The Yucheng victims who completed blood sample collecting for serum levels of PCB, PCDF, and PCDD congeners, and caffeine breath tests for CYP1A2 activity were enrolled. Six single nucleotide polymorphisms were selected for genotyping, including AhR (rs2066853), AhRR (rs2292596), ARNT (rs7517566), ARNT (rs3820541), ARNT (rs3768016), and ARNT (rs2228099).

Results AhRR (rs2292596) and ARNT (rs2228099) polymorphisms were significantly related to CYP1A2 inducibility. AhRR (rs2292596) GG genotype is associated with higher CYP1A2 inducibility compared to GC and CC. ARNT (rs2228099) GG genotype is associated with higher CYP1A2 inducibility compared to GC and CC. Both genotypic effects were dose-dependent. A joint effect was observed for AhRR (rs2292596) and ARNT (rs2228099) polymorphisms.

Conclusions Overall, AhRR (rs2292596) and ARNT (rs2228099) genotypes predict the CYP1A2 inducibility in people highly exposed to dioxin-like chemicals, and may play crucial roles in interpersonal variation in susceptibility to dioxin-related health effects.